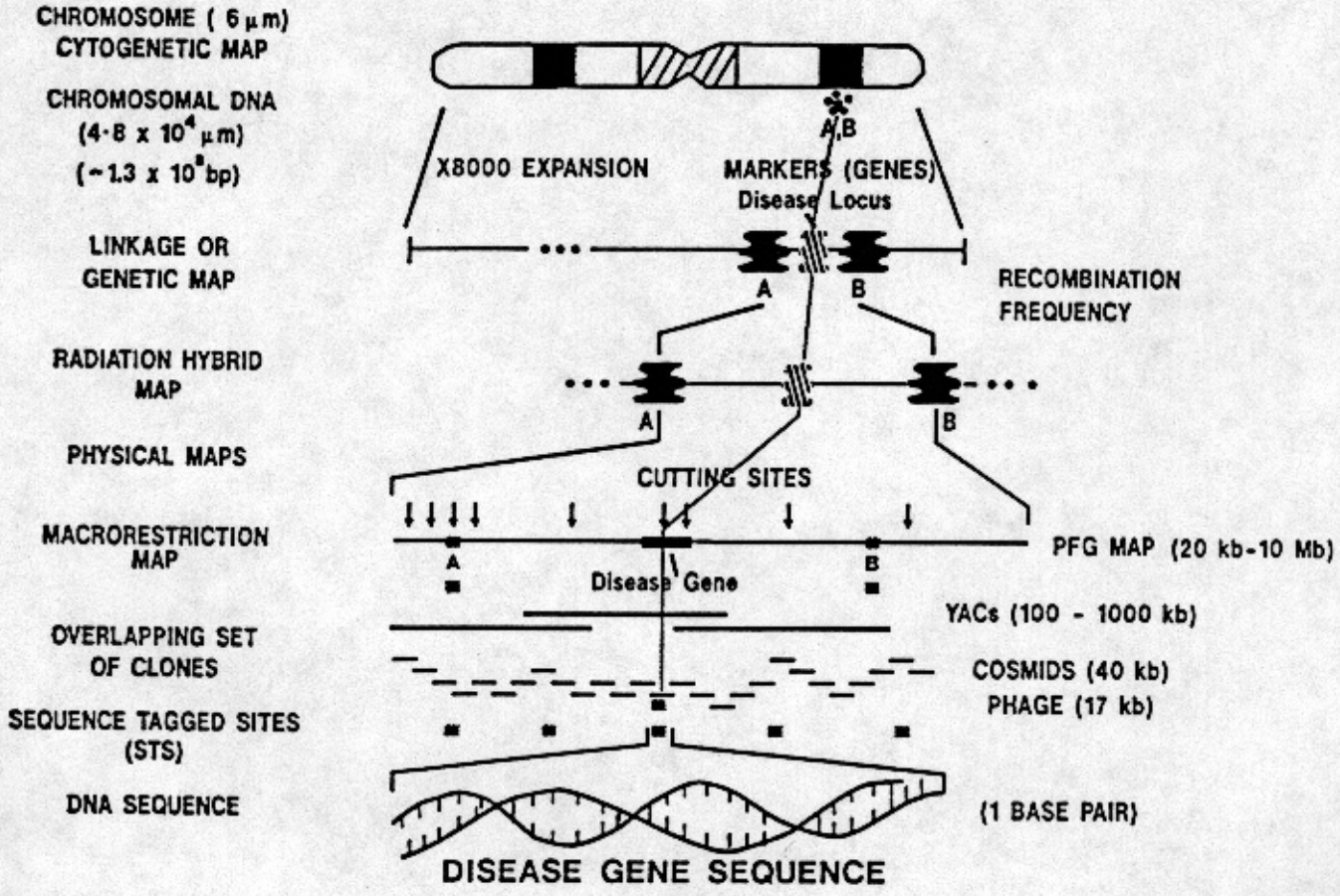
Genetics

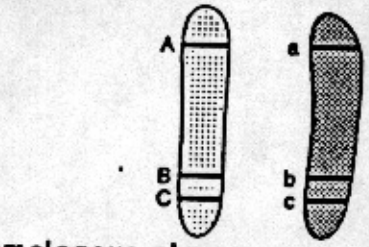
The biology of heredity, especially the study of ***hereditary transmission*** and ***variation***

(American Heritage Dictionary)

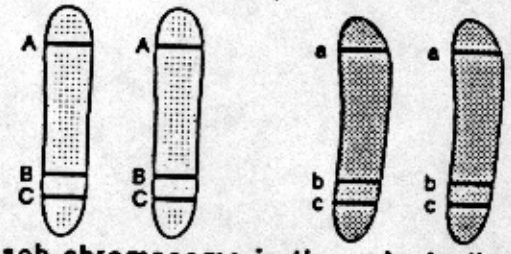


Multiple Levels of Human Chromosome Mapping. *The line running vertically through the diagram represents the tracking of markers A and B through progressively more precise levels of mapping. In this way, investigators can follow a candidate disease gene from the coarsest to the finest map resolution, which is the DNA sequence. The cytogenetic map provides the lowest level of resolution, measuring the distance between chromosomal features (i.e., bands or breakpoints) visible under the light microscope. Chromosome banding can resolve features to about 5 Mb. The linkage or genetic map measures the recombination frequency between two linked markers, which can be genes or polymorphisms (A and B in this diagram.) Radiation hybrid maps are produced by breaking chromosomes with radiation and then identifying the fragment carrying the marker (the breakpoint); the resolution of these maps is comparable to that of linkage maps. At the next resolution level, macrorestriction fragments of 1 to 2 Mb are separated and the markers localized and mapped. Finer mapping resolution is provided by ordered libraries of yeast artificial chromosomes (YACs), which have insert sizes from 100 to 1000 kb. Ordered libraries of cosmids have smaller insert sizes, usually about 40 kb, and produce higher-resolution maps. The DNA base sequence is the highest-resolution map, with sequence tagged sites (STSs) used as unique reference points. (Figure provided by C. E. Hildebrand, LANL.)*

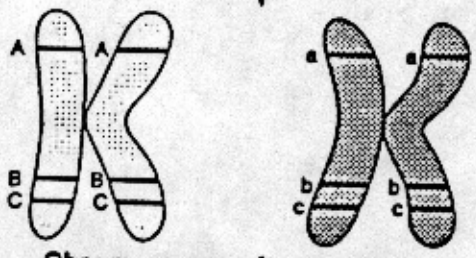
Figure 2-5.—Separation of Linked Genes by Crossing Over of Chromosomes During Meiosis



Homologous chromosomes come together in pairs before haploid sex cells are formed in meiosis.

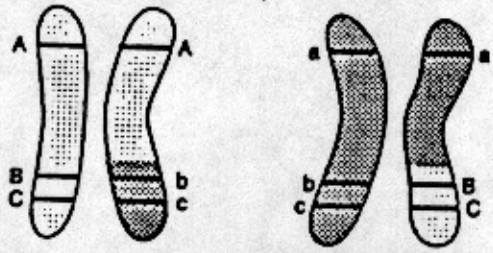


Each chromosome in the pair duplicates itself.



Chromosomes form synapses.

Crossing over upon breaking and rejoining of chromosomes.

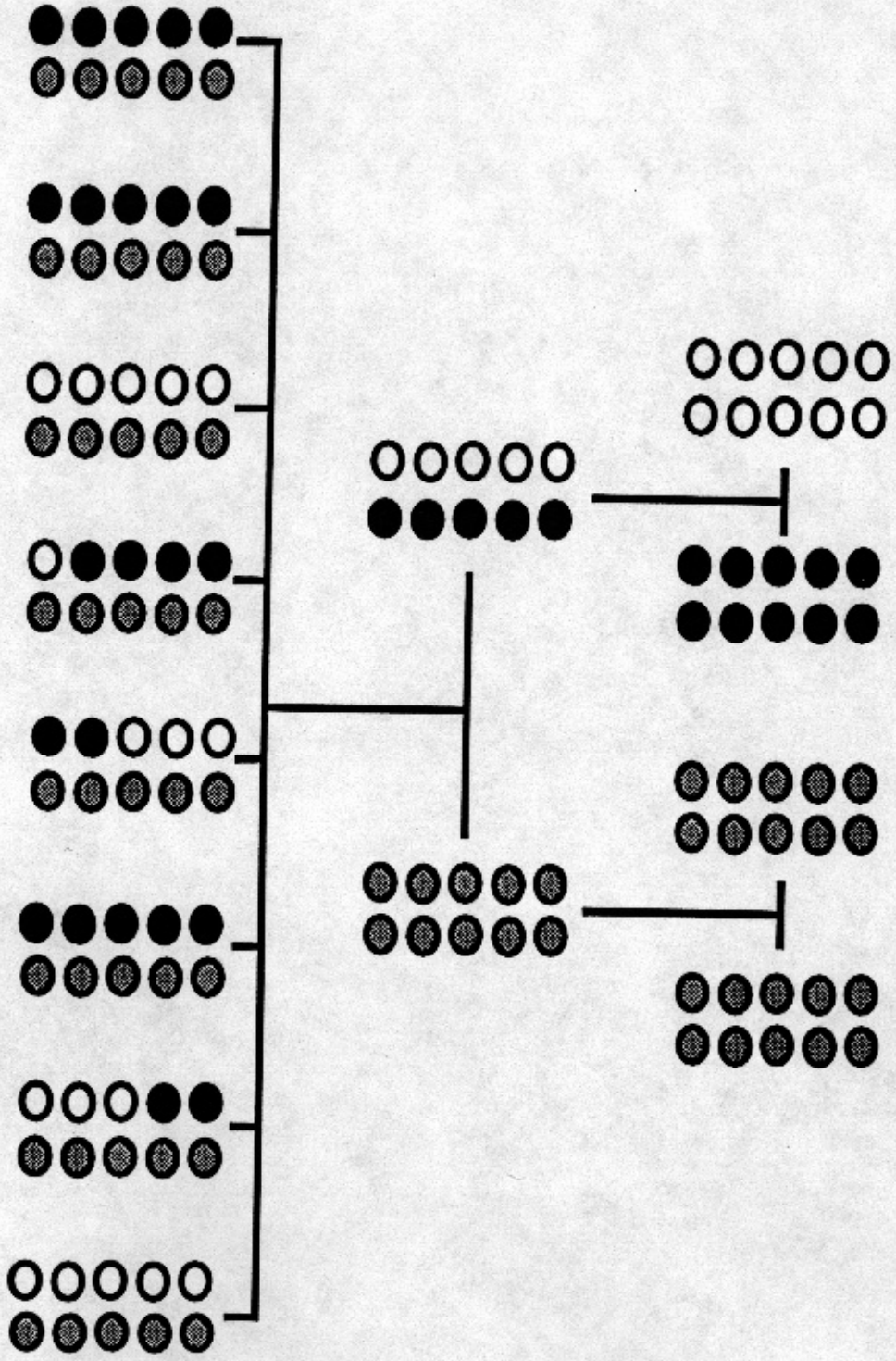


Chromosomes with new gene combinations after crossing over.

SOURCE: Office of Technology Assessment, 1988.

Alternative (gel-free) genotyping approaches

- OLA
- GBA
- TaqMan
- DNA chips



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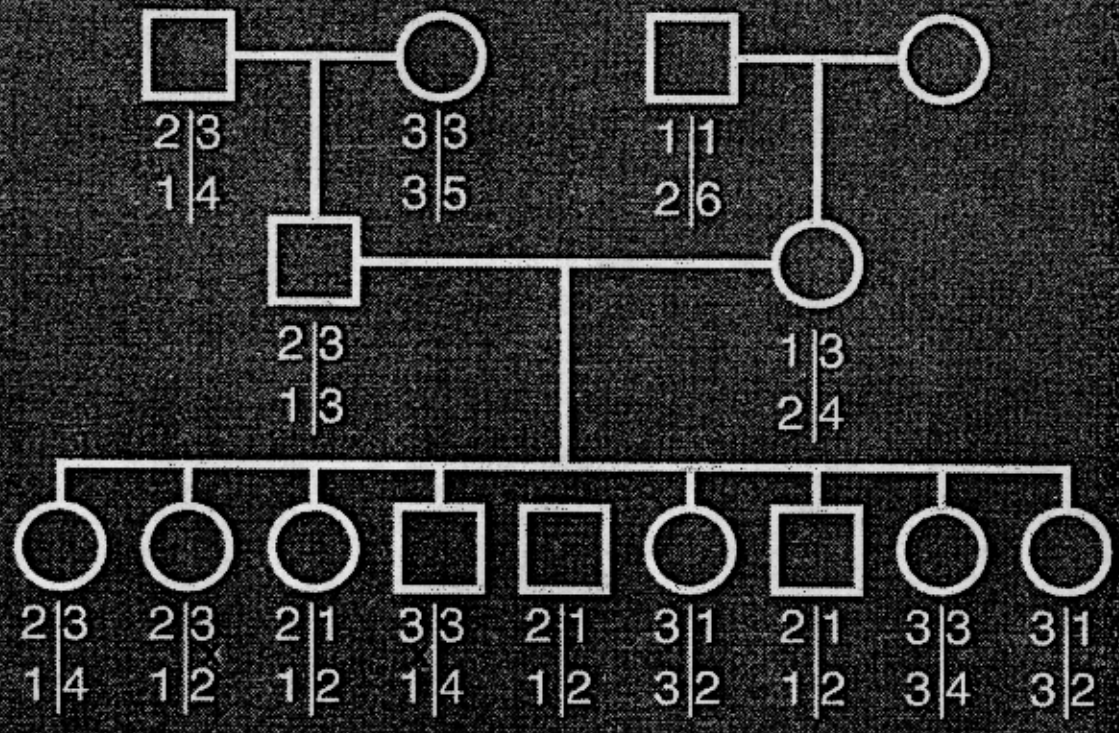

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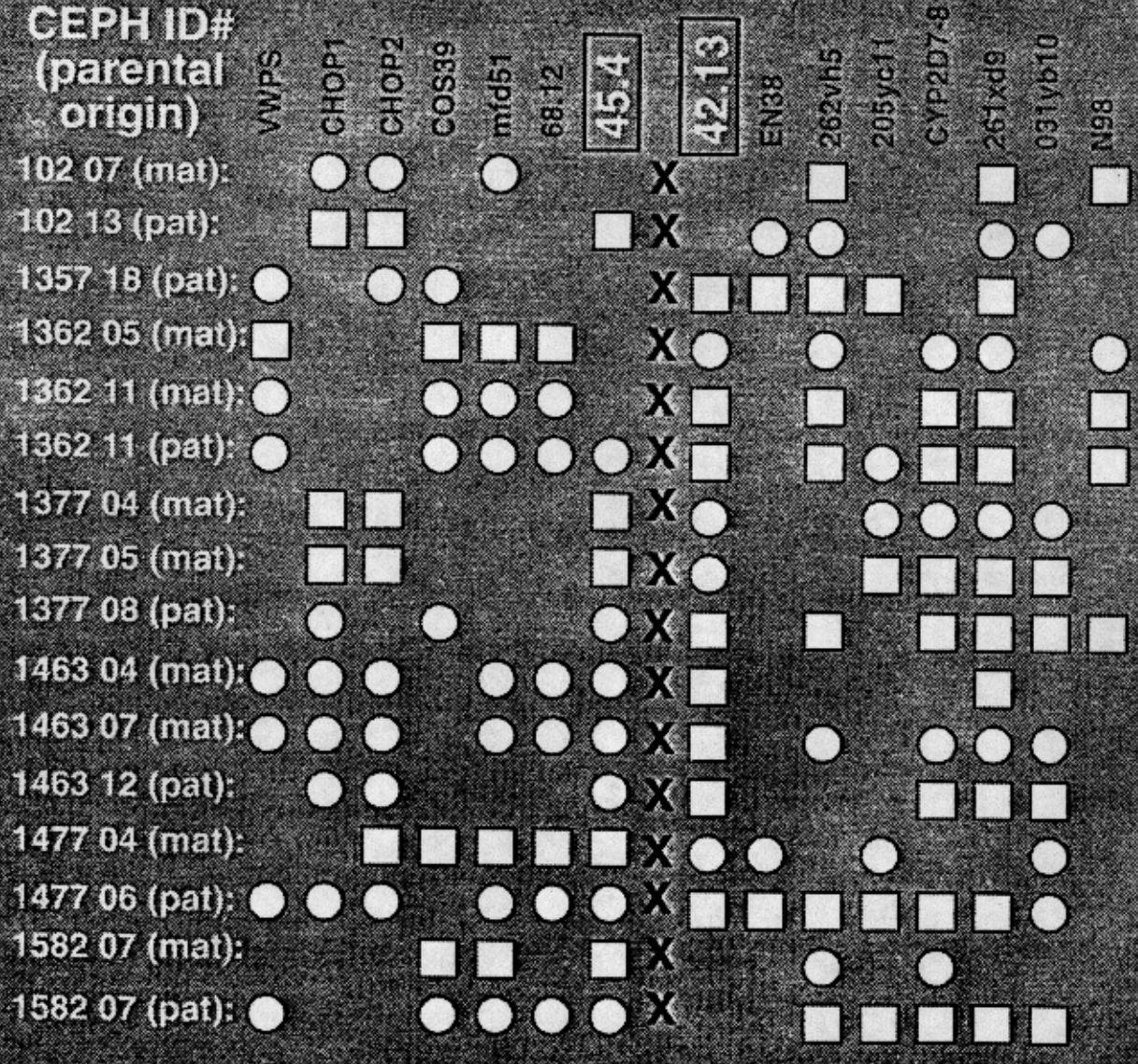
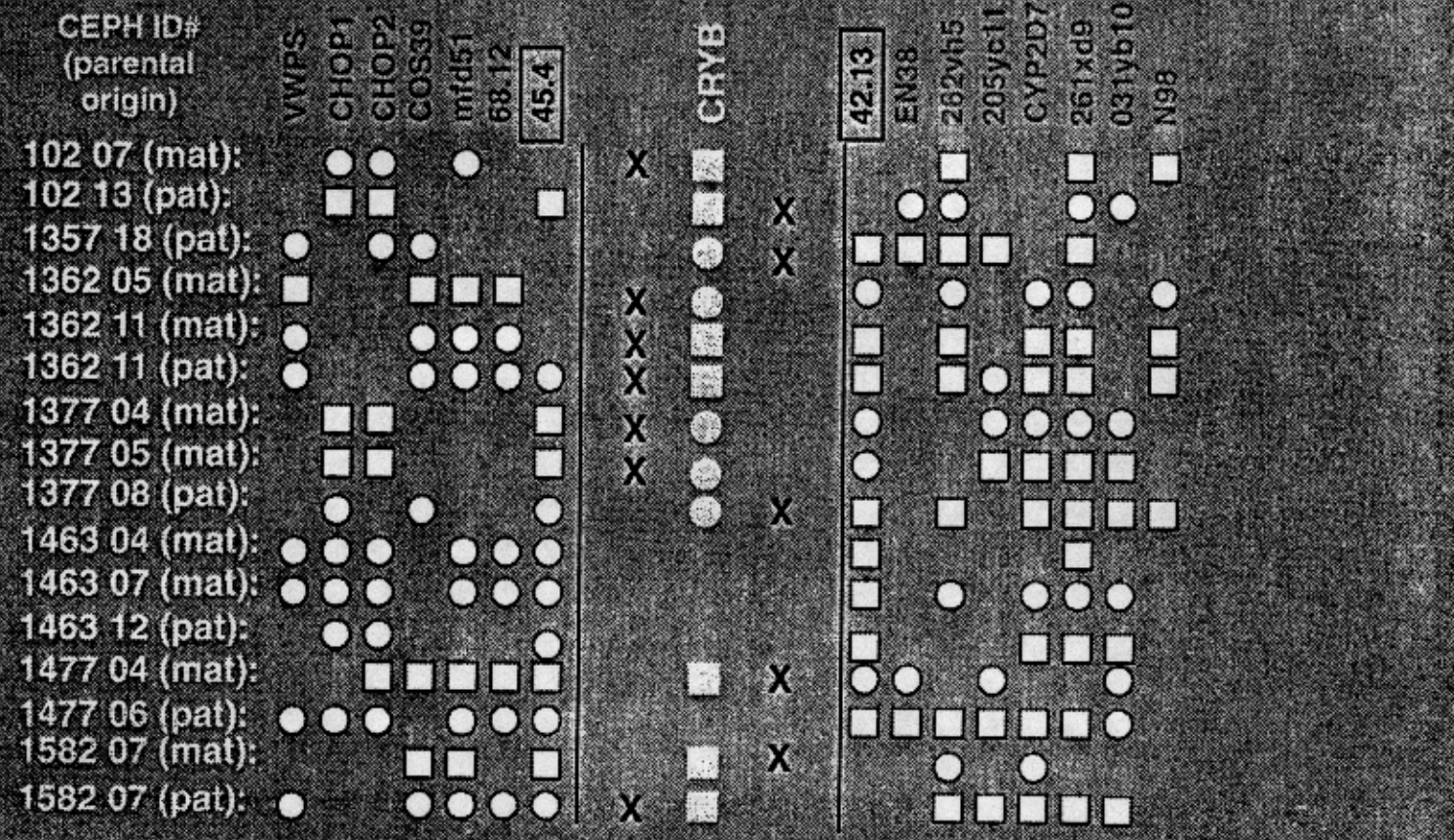
Recombinant Interval Database

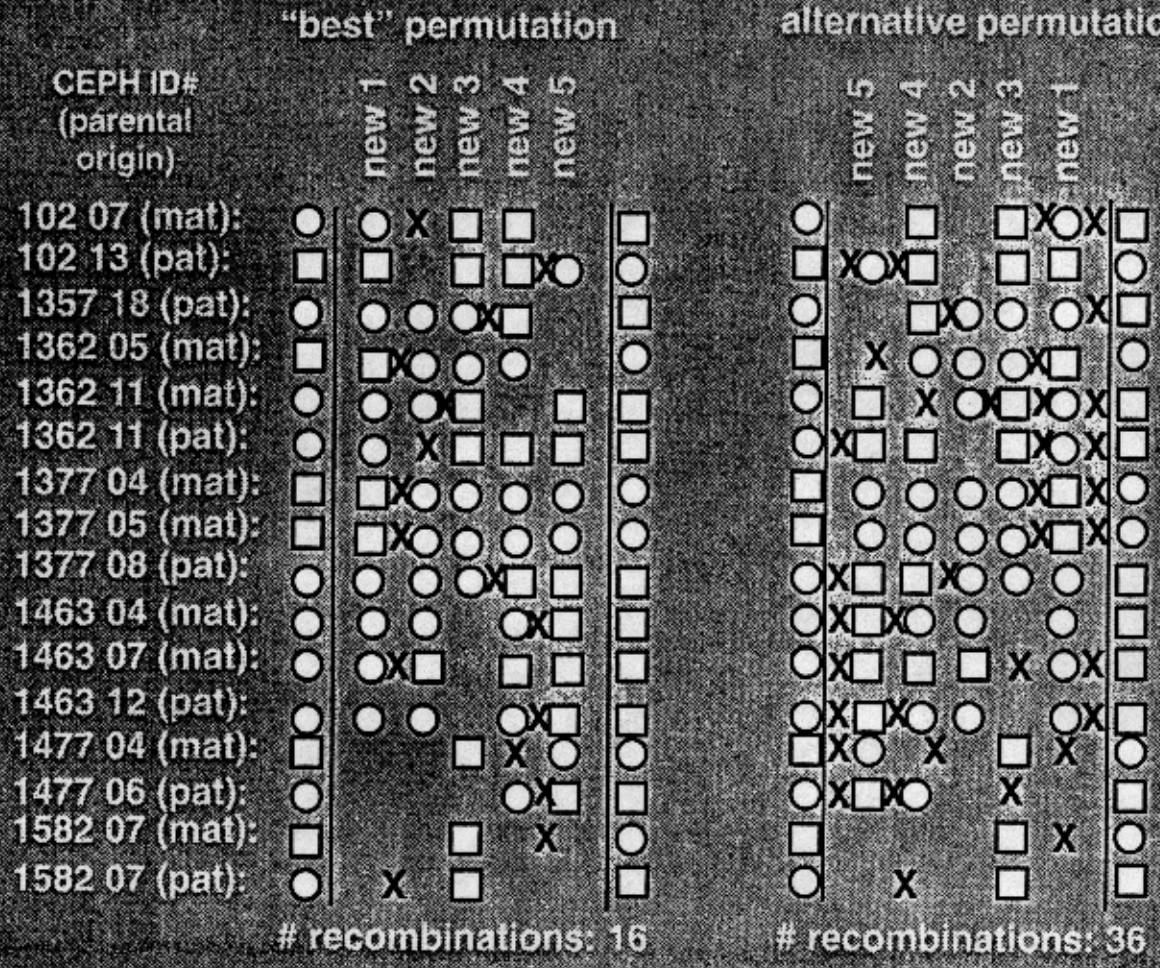
recombinant haplotypes from index map for marker interval:



Updated Reference Map Using Recombinant Interval Database



bin ordering by recombination minimization



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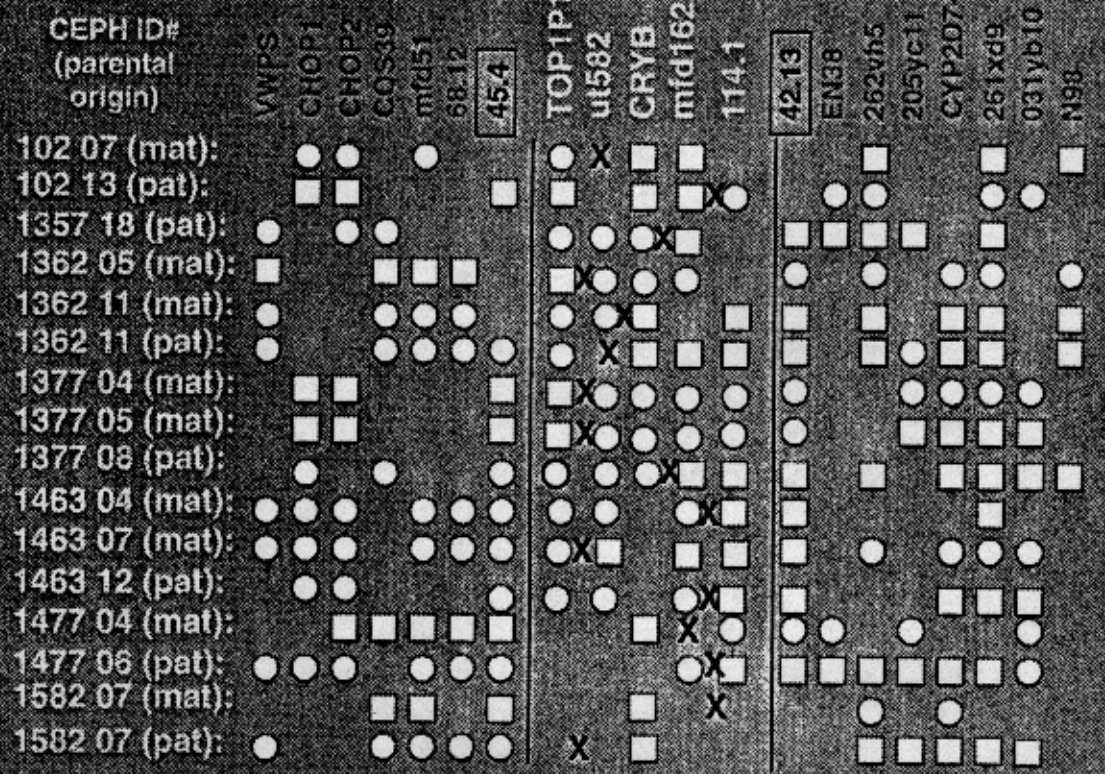

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